

In view of the foregoing, applicant maintains that the claims are enabled, and respectfully requests that the rejection under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

The rejection of claims 43 and 47 under 35 U.S.C. §102(b) as anticipated by Verma et al. (Cardiovascular Research 34:121-128, 1997) is respectfully traversed. The Examiner stated that "Verma, S. et al. disclose a method wherein hypertensive rats are administered mibefradil, a T-type calcium channel blocker, with a resultant decrease in insulin secretion, which would necessarily be a decrease in insulin secretion by the rat beta cells." Applicant respectfully traverses this rejection.

The claims herein are directed to a method of modifying insulin secretion by pancreatic beta cells by modifying levels of functional T type calcium channels in the pancreatic beta cells. Referring to page 126 of Verma et al., right column, first full paragraph, the authors state that "if mibefradil were to decrease insulin release, it would in turn lead to hyperglycemia, which was not the case . . . it is reasonable to suggest that the effects of the drug [mibefradil] on insulin levels were independent of changes in pancreatic insulin release." Thus, Verma et al. explicitly teach away from the subject invention which is based on the discovery that T type calcium channels in pancreatic beta cells directly affect insulin secretion by pancreatic beta cells.

Further, Verma et al. does not teach or suggest a method of modifying insulin secretion in vitro, because Verma relates to animal models.

Therefore, applicant maintains that Verma et al. does not teach or suggest, much less render anticipated, the claims herein. Accordingly, applicant respectfully requests that this rejection be reconsidered and withdrawn.

The rejection of claims 43 and 47 under 35 U.S.C. §102(a) as anticipated by Bhattacharjee et al. (Endocrinology 138(9):3735-3740, 1997) is respectfully traversed. Without addressing the substantive issues of this rejection, applicant points out that the cited reference is from the September 1997 issue of Endocrinology and is a reference of applicant that was published less than a year before applicant's effective filing date (August 26, 1998).

Therefore, applicant maintains that the Bhattacharjee et al. reference is not available as prior art against the subject invention and respectfully requests that this rejection be reconsidered and withdrawn.

The rejection of claim 43 under 35 U.S.C. §102(b) as anticipated by Kato et al. (Metabolism 43(11):1395-1400, 1994) is respectfully traversed. The Examiner alleges that Kato et al. disclose "a method wherein neonatal rats are treated with streptozocin, increasing the level of functional T-type calcium channels, evidenced by the increased  $Ba^{2+}$  induced currents, and increasing insulin secretion." Applicant respectfully traverses this rejection.

The claims herein are directed to a method of modifying insulin secretion by pancreatic beta cells by modifying levels of functional T type calcium channels in the pancreatic beta cells. Referring to page 1398 of Kato et al., right column, first full paragraph, the authors are discussing rat pancreatic  $\beta$  cells and conclude that the role of "T-type  $Ca^{2+}$  channels in the excitation-secretion coupling of  $\beta$  cells is still unknown." Thus, Kato et al. explicitly teach away from the subject invention which is based on the discovery that T type calcium channels in pancreatic beta cells directly affect insulin secretion by pancreatic beta cells.

Therefore, applicant maintains that Kato et al. does not teach or suggest, much less render anticipated, the claims herein. Accordingly, applicant respectfully requests that this rejection be reconsidered and withdrawn.

Formal drawing (15 sheets) are enclosed herewith.

In view of the above amendments and remarks, applicant maintains that the claims as amended herein define patentable subject matter. A notice of allowance is therefore requested.

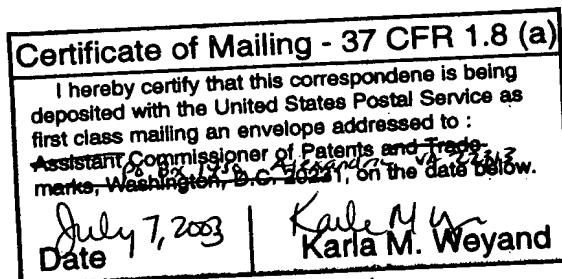
Pursuant to 37 CFR §§ 1.97-1.98, applicants submit herewith to the U.S. Patent and Trademark Office copies of the references listed on the attached PTO-1449 form.

Respectfully submitted,

July 7, 2003  
Date

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**Appendix-Marked-up version of the claims:**

43. (Amended) A method of modifying insulin secretion by pancreatic beta cells in vitro, the method comprising modifying levels of functional T type calcium channels in the in vitro pancreatic beta cells.